

**Durant, James T. (ATSDR/DCHI/SSB)**

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**From:** Verbrugge, Lori (CDC alaska.gov)  
**Sent:** Tuesday, December 08, 2009 1:16 PM  
**To:** Brewer, Marlena M (DEC); Farris, Ann M (DEC); Janes, William B (DEC); Crapps, Earl L (DEC)  
**Cc:** Durant, James T. (ATSDR/DTEM/PRMSB)  
**Subject:** RE: Sulfolane info from Superfund

Thanks, Marty! I appreciate this. It is helpful to have EPA's clarification on the uncertainty factors they would normally use under their guidelines; I had also thought that 10-fold UF was more appropriate than 3-fold for the sub-chronic to chronic extrapolation. I'm passing this analysis on to Jim at ATSDR for them to use in their assessment, which should be out very soon.

*Lori Verbrugge, Ph.D.*

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**From:** Brewer, Marlena M (DEC)  
**Sent:** Monday, December 07, 2009 5:09 PM  
**To:** Verbrugge, Lori Ann (HSS); Farris, Ann M (DEC); Janes, William B (DEC); Crapps, Earl L (DEC)  
**Subject:** FW: Sulfolane info from Superfund  
**Importance:** High

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**From:** Prues.Amy@epamail.epa.gov on behalf of SUPERFUND\_STSC@epamail.epa.gov  
**Sent:** Mon 12/7/2009 7:02 AM  
**To:** Brewer, Marlena M (DEC); Bailey.Marcia@epamail.epa.gov  
**Cc:** cubblson.chris@epamail.epa.gov; Mukerjee.Debdas@epa.gov; Zhao.Jay@epamail.epa.gov; Reid.Jon@epamail.epa.gov; Shannon.Teresa@epamail.epa.gov; Heing.Dan@epamail.epa.gov  
**Subject:**



Marcia and Marlena,

One of our scientists, Dr. Debdas Mukerjee, researched sulfolane toxicity. He ordered copies of the key studies used by Environment Canada to derive a Tolerable Daily Intake (TDI). He reviewed the study methods as well as the Canadian methods for deriving the TDI. Further, he obtained an original copy (in Chinese) of the Zhu et al. (1987) paper and another of our scientists, Dr. Zhao, reviewed the study for its utility in risk assessment. He found an error in one of the values used in the Canadian assessment (that did not impact the assessment) but otherwise confirmed that the study methodology was valid. In summary, Dr. Mukerjee found the Canadian methods to be a reasonable approach to deriving TDIs and that the critical study, from Huntingdon Life Sciences, although unpublished, was supported by published

studies. His report, is below.

Region 10 requested opinion of the STSC whether the Tolerable Daily Intake (TDI) value recommended in the Scientific Supporting Document titled '*Canadian Environmental Quality Guidelines for Sulfolane: Water and Soil*' published in 2006 by Environment Canada is sufficiently credible and justifiable to evaluate impacted sources of drinking water.

No PPRTV on Sulfolane is available. No new studies on this were found in the literature search for toxicity studies published from 2003 to date.

Sulfolane is used for removal of acid gases from natural gas during gas exploration. Sulfolane is also used as a solvent in plasticizing, electrical/electronic, and textile industries. It is a colorless, highly polar, water-soluble compound. Sulfolane migrates easily through the soil strata and can contaminate the ground water.

Environment Canada reviewed Andersen et al., (1997) 90 day subchronic inhalation exposure study with rats, guinea pigs, beagle dogs and squirrel monkeys; Zhu et al., (1987) six month subchronic oral exposure study with guinea pig; and a 13 week subchronic oral exposure rat (both sexes) study by the Huntingdon Life Sciences (2001). Huntingdon Life Sciences (2001) rat study was used for developing a Tolerable Daily Intake (TDI) value for Sulfolane. The hard copy of this study was not available to STSC for review.

Zhu et al., (1987) study in Chinese was kindly translated for our use by an EPA toxicologist, Dr. Jay Zhao. Zhu et al., (1987) presented results from a six month oral subchronic exposure study in freshly weaned guinea pigs. In the males pathological examination revealed a clear dose-response changes of the liver. No statistical significance level of changes was mentioned by the authors. Zhu et al., (1987) also reported on a reproductive and development toxicity in mice. In this study Sulfolane was administered orally, once a day, from 6th to 15th day of pregnancy. N'-methylene-bis (2-amino-1,3,4-thia diazole) was used as a positive control in this study. In the highest exposed group (840 mg/kg) resorption of fetus was 30.16% compared to 13.53% in the negative control, not 10.53% as mentioned in the *Canadian Environmental Quality Guidelines for Sulfolane: Water and Soil* (2006) document. Abnormalities of the sternum and ribs were observed in the fetus of the highest dosed (840 mg/kg) group of dams.

From a review of the '*Canadian Environmental Quality Guideline for Sulfolane: Water and Soil*' (2006) document I found that the adverse effects observed in the Huntingdon Life Sciences (2001) study were nephropathy in male rats at the highest doses of 35 and 131.7 mg/kg/d and reduced white blood cell (WBC) counts in females in three highest doses of 10.6, 42, and 191.1 mg/kg/d. Reduction of WBC was consistent with another study by Andersen et al., (1977). Bone marrow suppression was also observed in Zhu et al (1987) subchronic study with guinea pigs. NOAEL for nephropathy was 8.8 mg/kg/d in male rats and NOAEL for reduction of WBC was 2.9 mg/kg/d in female rats. TDI of 0.0097 mg/kg/d for Sulfolane was developed using the NOAEL of 2.9 mg/kg/d for WBC reduction in female rats applying a combined UF of 300 (10 for interspecies differences, 10 for human variability, and 3 for subchronic to chronic extrapolation). In accordance with the EPA's Risk Assessment Guidelines, for subchronic to chronic extrapolation a full UF of 10 would have been used due to lack of chronic data and inadequate reproductive and developmental study data. Consequently, the combined UF would have been 1000 instead of 300. However, in absence of any assessment value by EPA, I feel it is reasonable to use the Canadian value to evaluate impacted sources of drinking water.

I hope this helps you with the Sulfolane situation. As always, feel free to contact the STSC if you have any questions or concerns regarding this request.

Sincerely,

Amy Prues  
STSC